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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 15

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Application Number: 09/724,135
Filing Date: November 28, 2000
Appellant(s): MCFARLAND, EILEEN LOUISE RICE

Alice O. Carroll
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 9, 2002.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

This appeal involves claims 1-13.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The amendment after final rejection filed on September 9, 2002 has been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because applicant has not grouped claims 11 and 13 with an explanation of the claims with which they stand or fall.

(8) Claims Appealed

A substantially correct copy of appealed claims 1-13 appears on pages 11-12 of the Appendix to the appellant's brief. The minor errors are as follows:

In claim 1, line 1, "the diagnosis" should be "a diagnosis."

In claim 5, "a blood type which is the same" should be "compatible blood type."

In claim 6, line 5, "schizophrenia" should be "psychosis."

In claim 11, line 1, "the diagnosis" should be "a diagnosis."

Applicant has not incorporated the after final amendments into the copy of the appealed claims in the appendix.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's invention is drawn to a method of determining predisposition to psychosis by measuring the presence of anti-Cw antibodies in a sample. However, many dispositions, outside the realm of psychotic disorders may be determined by measuring these antibodies. For example, numerous studies, including Curtin et al., (Am. J. Medical Tech., 1967) Mouro et al. (Blood, 1995), and Bowman et al. (Vox Sang, 1993) disclose the measurement of these antibodies for the determination of hemolytic disease. Therefore, how can the determination of the same antibodies be used to determine psychosis with the exclusion of other disorders related to cw antibody presence? The current state of the art does not enable the undertaking of a method or kit for this purpose. Further, since Cw is relatively rare and no previous definitive correlation has been demonstrated between the measurement of cw antibodies and psychosis, a method attempting to link the two inherently encompasses a great amount of uncertainty, which the current state of the art is unable to

remedy. In addition, there is insufficient guidance and working examples in the specification to enable one of skill in the art to determine predisposition to psychosis by measuring anti-cw antibodies. The one case study with only 1 subject referenced in the specification is grossly insufficient to meet this criterion of enablement. The results from one case study cannot possibly be used as a definitive statement that the method of applicant can be used in all cases and populations to determine predisposition to psychosis. Results of case studies must be readily reproducible, which has not been established in this instance. Especially when considering that only one patient was followed in the case study, the onset of schizophrenia could have occurred by chance and not due to the presence of anti-cw antibodies. In addition, the disclosure of applicant has not enabled the determination of predisposition to all types of psychosis. Since the many psychotic disorders affect the body through different mechanisms that may differ greatly, it is unclear how one could use one method to determine predisposition to all these disorders. Applicant has certainly not elucidated that issue in the specification. Further, applicant has only provided one example with a patient who developed schizophrenia, which is insufficient to enable all types of psychosis. Therefore, undue experimentation would be required of one of skill in the art to practice the invention commensurate with the full scope of the claims.

(11) Response to Argument

The examiner understands applicant's position to be that a correlation between anti-Cw antibodies in the mother and psychosis in progeny exists. The lone subject in the lone case study provided by applicants in support of their position involves a male whose mother's hemolytic status was not determined and/or stated. If the mother had hemolytic

disease in addition to the presence of anti-Cw antibodies, and her son coincidentally developed schizophrenia, to assert that the schizophrenia was a result of the presence of the anti-Cw antibodies in the mother is scientifically flawed. Anti-Cw antibodies are a known risk factor for hemolytic disease, but one cannot make the leap that just because the progeny may have developed psychosis, that anti-Cw antibodies were the reason. Applicant could have simply employed a sample of mothers with anti-Cw antibodies and hemolytic disease and selected the one progeny that developed psychosis. In no way does this entail a definitive relationship between anti-Cw antibodies and psychosis, as this may have resulted from pure chance.

Applicant argues that the Mouro, Curtin, and Bowman references, which are used as support in asserting that the claimed invention is enabled, do not teach applicant's invention. The examiner acknowledges this fact, as these references were not applied under 35 USC 102 and/or 35 USC 103. Although the examiner agrees that the hemolytic diseases discussed in these references may be indicative of the adverse effects of histocompatability, the examiner maintains that one cannot differentiate between psychosis and hemolytic disease based on the claimed method of applicant, which was the only reason that these references were cited. Also, although applicant states that it is not necessary to differentiate between psychosis and hemolytic disease, the utility of the claimed method is for determining predisposition to psychosis, not hemolytic disease, so some differentiation between the two is indeed necessary. Further, applicant asserts that a link has been established between pregnancy complications and mental illness; however, as the claimed

method does not recite pregnancy complication in any way (and applicant has not asserted that presence of Cw antigen is a complication), the basis of this assertion is not understood.

Applicant acknowledges that the claimed method ***can be*** indicative of a predisposition to psychosis, which inherently indicates that the claimed method may not work. For the invention to be enabled, the claimed method must work. Applicant direct the Board to the Wright reference in asserting that a link between HLA histocompatability and psychosis has been established; however, the examiner notes that the Wright reference specifically states, "a susceptibility locus ***may exist*** and it ***may be*** within the HLA region, but again the evidence is ***far from conclusive***". This disclosure in the reference clearly indicates that no such link has been definitively established, but rather, merely postulated.

With respect to the Chowdari reference, it is noted that the authors indicate that their results suggest a susceptibility locus for schizophrenia in the HLA region, but their results are limited to the Chinese, and they acknowledge that further clarification is necessary. They also state that "an autoimmune pathology for schizophrenia is plausible, though persuasive evidence is unavailable", and genome linkage studies "have not yielded consistent results for schizophrenia". They also state that "the question of HLA association with schizophrenia is unresolved".

Applicant further asserts that the case study disclosed in the application, in combination with the state of the art, is sufficient to enable the present invention. Applicant cites several references in support of this contention. Regarding the Lindholm study, applicant argues that the reference reports the presence of a schizophrenia-susceptibility locus. However, this study only focused on one pedigree, and other genetic factors native to

that pedigree may have influenced onset of psychosis. The authors of this study also recognize the need for further study before drawing any definite conclusions about the relationship between the gene and schizophrenia.

Applicant also argues that the Bassett and Lahdelma references help support their claims of the enablement of the present claims because the references discloses associations between HLA and schizophrenia, thereby rendering the one case in applicant's specification sufficient to enable the claimed invention. The Bassett study states that a minority of patients with schizophrenia may have 22qDS, but they acknowledge that no casual genes have been identified and this is only one subtype of schizophrenia. Further, it is noted that the studies alluded to by Basset et al. in support of their contention only found one case and two cases, respectively, of schizophrenia with 22qDS. Both these studies employed sample sizes of less than 30, which precludes the obtainment of statistically significant results. One or two cases can easily be attributed to background prevalence of the gene. Basset et al. also acknowledge that many investigations are still necessary to determine the relationship of a 22qDS subtype to schizophrenia.

With respect to the Lahdelma reference, that study only employed subjects who already had schizophrenia. Therefore, no meaningful conclusions can be drawn about predisposition to a disorder if the patients already have the disorder. The proper temporal relationship has not been established. In addition, this study has little, if any relevance, to applicant's claims as the reference is only determining differences in treatment response between different groups of patients who already have a disorder. The reference still recognizes that studies have been unable to confirm the connection between HLA and

schizophrenia. Even Lahdelma et al. "could not find any altered frequency of HLA-A1 among schizophrenic patients in general". In addition, this study was only done on the Finnish population, and the authors recognize that the same association found in the study may not be found in other populations, which makes it impossible to extrapolate their results to create a general method of assessing predisposition to a psychotic disorder.

Applicant acknowledged that schizophrenia is a genetically complex disorder, with both genetic and environmental influences. Therefore, a case study on one individual clearly is insufficient to establish s link between Cw antigen and susceptibility to schizophrenia. In addition, although anti-Cw antibody may be one risk factor of the disease, people with this antibody may not develop the disease, and conversely, people without the antibody, may.

In addition, applicant argues that the case study provided is sufficient to enable the present invention, and undue experimentation is not required of the present invention. First, the examiner recognizes that working examples are not required to enable an invention; however, the presence of working examples in of several factors to be considered in determining enablement. The examiner disagrees with the assertion that undue experimentation is not required of the present invention. Although obtaining a biological sample and determining the presence of an antibody may in fact be routine, the claimed method does not end there. Rather, the claimed method requires a correlation to the onset of schizophrenia, the inset of which may take years or may never occur at all. Simply because one individual who had the antibody developed the disease, in no way is that sufficient to establish a link between the presence of anti-Cw antibody and psychosis.

Therefore, for the all the reasons discussed above, applicant's arguments that the state of the art allows for the practice of their invention without undue experimentation, thereby rendering the claimed invention enabled, is unconvincing. In fact, an association between anti-Cw antibodies and predisposition to psychosis has not been established with any consistency. Further, it is noted that the present claims are not restricted to specific populations, or even to schizophrenia, to which applicant's discussion was primarily limited. The examiner maintains the position that although undue experimentation would not be required to measure anti-Cw antibodies, it would be required to establish a definitive or any causal link between those antibodies and a predisposition to psychosis. Even in the one example provided by applicants, a number of years were required before a diagnosis of schizophrenia was made. In addition, the state of the art does not enable the diagnosis of a predisposition to psychosis. As applicant acknowledges, the prior art does not establish a link between anti-Cw antibodies and psychosis. Applicant's reliance on the case study present in the specification is insufficient to provide adequate predictability, guidance, and working examples. As discussed previously, applicant has shown the results of one individual possessing anti-Cw antibodies who later developed schizophrenia. This result may have occurred by chance. Since a study of many individuals from multiple studies has not been provided, applicant has not enabled the determination of a predisposition to psychosis. Further, applicant's arguments that the effect of the anti-Cw antibody and not the mere presence of the antibody is the determining factor is also unconvincing to provide enablement for the recited claims. The presence of the antibody renders the fact that it will exert some effect inherent.

In view of Applicant's amendment after final, the rejection of claims 1-5 and 11 under 35 U.S.C. 112, second paragraph, is herein withdrawn.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Kartic Padmanabhan
Patent Examiner
Art Unit 1641

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November 18, 2002

Conferees
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